

CALIFORNIA DEPARTMENT OF PESTICIDE REGULATION

PUBLIC REPORT 2004-2

Etoxazole
Tracking ID 199258N

DESCRIPTION OF ACTION

Valent USA Corporation submitted an application seeking California registration of TetraSan™ 5 WDG, EPA Reg. No. 59639-108, to control spider mites on greenhouse-grown ornamental plants and non-bearing fruit and nut trees. This product contains the new active ingredient etoxazole. TetraSan™ 5 WDG was conditionally registered by the United States Environmental Protection Agency (U.S. EPA) on August 22, 2002.

The Department of Pesticide Regulation (DPR) evaluated the product label and scientific data supporting registration of this product and found them to be acceptable to support conditional registration. The acute health risks from exposure to etoxazole are minimal due to its low mammalian toxicity. Precautionary and first aid statements on the product label, as well as label directions requiring work clothing and other protective measures adequately mitigate potential health risks to persons who may come in contact with the pesticide during the period of conditional registration. DPR does not expect significant adverse environmental impacts to result from registration of this product.

BACKGROUND

| | |
|-----------------------|---|
| Registrant: | Valent USA Corporation |
| Common name: | Etoxazole |
| Chemical name: | 2-(2,6-difluorophenyl)-4-[4-(1,1-dimethylethyl)-2-ethoxyphenyl]-4,5-dihydrooxazole |
| Brand names: | TetraSan™ 5 WDG |
| Uses: | Mite control on ornamental plants and non-bearing fruit and nut trees grown in greenhouses, shade and lath houses |
| Pests controlled: | Spider mites |
| Type of registration: | Conditional Registration for 18 months |

TetraSan™ 5 WDG is formulated as a water dispersible granule containing 5% etoxazole. It is packaged in 2 oz. water-soluble packets for ease in mixing and to reduce worker exposure during mixing and loading. TetraSan™ 5 WDG is registered to control spider mites infesting indoor (greenhouse, lath and shade house) grown ornamental crops including flowering and foliage crops, ground covers, shrubs and trees and non-bearing fruit and nuts trees. Etoxazole is a member of the oxazoline class of insecticides. It kills mite eggs and nymphs and prevents adults from laying viable eggs. Etoxazole is readily absorbed by the plant and will translocate locally in the leaf. TetraSan™ 5 WDG should be used early in infestations when the mite populations are low. A maximum of two applications are allowed per crop or within a six-month period. Applications are recommended at 8-16 oz. of product per 100 gallons of water applied as a full

coverage spray. Application through an irrigation or chemigation is prohibited. TetraSan™ 5 WDG should be used in rotation with other miticides in an integrated pest management program.

SCIENTIFIC REVIEW

A. Chemistry

1. Product Chemistry: DPR evaluated the submitted chemistry studies for TetraSan™ 5 WDG and the results are summarized in the following table.

Table I. Physical and Chemical Properties of TetraSan™ 5 WDG

| Properties | Values |
|---------------------|--|
| Physical state | Brown solid |
| Bulk density | 34.2 lb/ft ³ |
| PH (1% suspension) | 5.9 |
| Solubility (water)* | 7.04 x 10 ⁻² parts per million (ppm) at 20° C |
| Vapor pressure* | < 1 X 10 ⁻⁷ mm Hg at 25° C |
| Henry's law* | < 6.72 x 10 ⁻⁷ atm. m ³ /mole at 20° C |
| Storage stability* | One year at ambient temperature |

*These properties were derived using technical etoxazole as the test substance.

2. Residues in Food and Animal Feed: The TetraSan™ 5 WDG label does not include any food or feed uses. Therefore, residue data are not required to support registration of the product.
3. Environmental Fate: The etoxazole environmental fate studies reviewed included: soil adsorption/desorption, hydrolysis, aqueous and soil photolysis, aerobic soil metabolism, anaerobic aquatic metabolism, and field dissipation studies. The studies were found to be satisfactory. Soil adsorption/desorption studies were conducted in four sandy loam soils and the K_{oc} values indicate etoxazole is immobile in soil. The hydrolysis study was conducted in water with pHs at 5, 7, and 9 for a period of 21-30 days. Under acidic conditions etoxazole is hydrolyzed at a moderate rate with a half-life of 10 days (estimated with linear regression). However, in neutral to lightly alkali conditions, etoxazole resists hydrolysis and is almost stable with a 165 day half-life. Etoxazole reaction to sunlight (photolysis) is similar in water and soil. Its half-life in water ranges from 16-17 days and 22-25 days in soil. The aerobic soil metabolism study indicated that etoxazole is relatively unstable with a half-life of 19-24 days. With anaerobic water conditions, the estimated half-life (linear regression) was 133-142 days. Two terrestrial field dissipation studies were reviewed and the results indicate etoxazole has a short half-life in soil (18 days in the California study and 8 days in the Mississippi study).

The submitted product and environmental fate data support registration of the subject product. The data indicate etoxazole is unlikely to leach into groundwater because its water solubility is low and it is bound tightly to soil particles. In the soil etoxazole dissipates readily and should not accumulate. The use of etoxazole is expected to have minimal impact on the environment and it is not expected to leach into groundwater.

B. Toxicology

Valent USA Corporation submitted adequate toxicology studies to conduct a complete toxicological evaluation of TetraSan™ 5 WDG. DPR evaluated the submitted data to ascertain the potential for adverse health effects. The acute toxicity parameters for TetraSan™ 5 WDG are summarized in the following table.

Table II. Acute Toxicity of TetraSan™ 5 WDG

| Type of Study | Acute Toxicity Values | Acute Toxicity Category |
|---------------------------|----------------------------------|-------------------------|
| Acute Oral | LD ₅₀ (M/F) 4.27 g/kg | III |
| Acute Dermal | LD ₅₀ (M/F) 5.0 g/kg | IIV |
| Acute inhalation | LC ₅₀ (M/F) 2.05 mg/L | IIV |
| Primary eye irritation | N/A | III |
| Primary dermal irritation | N/A | IV |
| Dermal Sensitization | N/A | Not a sensitizer |
| Signal word | N/A | CAUTION |

DPR's evaluation of the acute toxicity data indicates that TetraSan™ 5 WDG is low in mammalian toxicity. The precautionary language on the product label adequately identifies the acute toxicity hazards noted in the studies.

DPR found the submitted toxicology studies adequate to satisfy the data requirements of the Birth Defects Prevention Act (Food and Agricultural Code section 13121 *et. al.*). A possible adverse health effect was observed in the mouse lymphoma assay for genotoxicity. A neurotoxicity study is not required at this time. DPR has not yet prioritized etoxazole for risk assessment. DPR prioritizes pesticide active ingredients for risk assessment based on the nature of the potential adverse health effects, number of potential adverse health effects, number of species affected, NOELs, potential for human exposure, use patterns, and similar factors. Based on these criteria, pesticides with the greatest potential for health problems are placed in high priority, with other chemicals being place in moderate or low priority. The purpose of the risk assessment will be to appraise the potential for etoxazole to cause adverse health effects in humans if exposed to the pesticide as the result of a legal use. Further toxicity information is available in DPR's Summary of Toxicology Data for etoxazole, available on DPR public website at <http://www.cdpr.ca.gov/docs/toxsums/pdfs/5849.pdf>

C. Health & Safety

An evaluation of the medical management information on the TetraSan™ 5 WDG label and the acute toxicity study results indicate that the product labels bear all of the required statements and warnings regarding safety to handlers and other persons who may be exposed to the pesticide. The product label bears an adequate First Aid statement. In addition, the product label requires persons handling and applying TetraSan™ 5 WDG to wear long-sleeved shirt and long pants, and shoes plus socks. Workers wearing only work clothing are not allowed to enter a treated field until 12 hours after an application. The product label requires that persons entering a treated area before the 12-hour restricted-entry interval (REI)

has elapsed must wear coveralls, waterproof gloves and shoes plus socks if they are going to contact treated plants, soil or water.

D. Fish & Wildlife

The registrant submitted fish and wildlife toxicity studies, including studies on rats, bluegill sunfish, bobwhite quail, *Daphnia magna*, honeybees, mallard ducks, Mysid shrimp, oysters, rainbow trout and sheepshead minnow. The submitted data are adequate to characterize toxicity to wildlife and aquatic animals from an environmental exposure. Table III summarizes the results of these studies.

Table III. Summary of Toxicity Studies for Wildlife

| Test Animal | Type of Study | Acute Toxicity Value | Relative Toxicity |
|----------------------|--------------------------|-----------------------------------|----------------------|
| Rat, female | Single acute oral dose | >2500 mg/kg (LD ₅₀) | Relatively non-toxic |
| Rat, male | Single acute oral dose | >4500 mg/kg (LD ₅₀) | Relatively non-toxic |
| Mallard duck | Single acute oral dose | >2000 mg/kg (LD ₅₀) | Relatively non-toxic |
| Mallard duck | Feeding study (8 days) | >5200 ppm (LC ₅₀) | Slightly toxic |
| Bobwhite quail | Feeding study (8 days) | >5200 ppm (LC ₅₀) | Relatively non-toxic |
| Bluegill sunfish | Water exposure (96 hrs.) | 1.4 mg a.i./l (LC ₅₀) | Moderately toxic |
| Rainbow trout | Water exposure (96 hrs.) | 2.8 mg a.i./l (LC ₅₀) | Moderately toxic |
| <i>Daphnia magna</i> | Water exposure (48 hrs.) | 7.1 ug a.i./l (EC ₅₀) | Extremely toxic |
| Sheepshead minnow | Water exposure (96 hrs.) | 160 ppb (LC ₅₀) | Highly toxic |
| Mysid shrimp | Water exposure (96 hrs.) | 4.4 ppb (LD ₅₀) | Extremely toxic |
| Oyster | Water exposure (96 hrs.) | 1.2 ppb (EC ₅₀) | Extremely toxic |
| Honeybee | Contact (48 hrs.) | >200ug/bee (LD ₅₀) | Relatively non-toxic |

•Acute toxicity values expressed as: a. LD₅₀= lethal dose that will kill 50% of test population, and b. LC₅₀= lethal environmental concentration that will kill 50% of test population.

•The test substance used for the studies was technical etoxazole.

The data indicate that etoxazole is relatively non-toxic to vertebrate animals, birds and honeybees, moderately toxic to fish, and extremely toxic to oysters and freshwater invertebrates. The proposed use pattern, in greenhouses, lath houses and shade houses, is not expected to result in contamination of aquatic environments. Terrestrial degradation studies indicate that etoxazole breaks down readily in soil and does not accumulate. In addition, the TetraSan™ 5 WDG label bears language warning against the contamination of water and intertidal areas below the mean high water mark. The use of TetraSan™ 5 WDG is not expected to pose a threat to wildlife when used in accordance with label directions.

E. Efficacy & Phytotoxicity

The submitted efficacy studies are limited in scope, but do indicate that TetraSan™ 5 WDG provides effective control of tetranychid mites on a few selected indoor-grown ornamental plants and non-bearing fruit and nut trees. However, the ability of TetraSan™ 5 WDG to penetrate various plant canopies and translocate in the leaves is not well defined. Additional efficacy data are needed to support the wide range of ornamental plants and non-bearing fruit

and nut crops listed on the label. Phytotoxicity studies indicate that TetraSan™ 5 WDG is not phytotoxic to a limited range of ornamental crops and non-bearing tree crops. However, some of the trials were not conducted at maximum label rates. In addition, a few of the tested plants did express sensitivity to, and injury from, TetraSan™ 5 WDG that may not be commercially acceptable. A conditional registration is recommended to allow the registrant time to generate additional efficacy and phytotoxicity studies.

ALTERNATIVES

TetraSan™ 5 WDG is not intended to be used as an alternative to other miticides but rather to be used in rotation with other miticides to control mite infestations and slow the development of resistance. Etoxazole is primarily active on mite eggs and larval stages and it will not kill adult mites. However, etoxazole has the unique ability to prevent adult mites from laying viable eggs. In addition, etoxazole is not toxic to predacious mites, which can then help to control mite infestations. Because TetraSan™ 5 WDG has a different mode of action, it can be used in rotation with carbamate, organophosphate and other miticides like pyridaben and propargite to slow resistance development.

CONCLUSION

DPR evaluated the product label and scientific data submitted to support the registration of TetraSan™ 5 WDG and found them acceptable to support conditional registration. The acute health risks to humans from exposure to etoxazole are minimal due in part to its low mammalian toxicity. The precautionary and first aid statements on the product label, as well as the required work clothing and other protective measures mitigate potential health risks to persons who may be exposed to the pesticide. If a risk assessment is conducted and DPR determines that exposure to etoxazole may result in unacceptable margins of exposure, further restrictions will be placed on the use of etoxazole at that time. The submitted data also indicate significant adverse environmental impacts are not expected to occur from the use of TetraSan™ 5 WDG. When used in accordance with label directions, this product will be effective for its intended use.

DPR is granting an 18-month conditional registration for TetraSan™ 5 WDG. The registrant is required to submit additional phytotoxicity data from studies where applications were made at the maximum label rate on ornamental shrubs and trees, non-bearing fruit and nut trees. Additional efficacy data are also needed from each group (bedding plants, flowering plants, etc.) to evaluate the ability of a TetraSan™ 5 WDG application to penetrate different types of leaf canopies and translocate in the leaves.